

EXHIBIT 1

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS**

ABBOTT GMBH & CO., KG,)
ABBOTT BIORESEARCH CENTER, INC.,)
AND ABBOTT BIOTECHNOLOGY LTD.,)

C.A. No. 4:09-CV-11340 (FDS)

Plaintiffs,)

JURY TRIAL DEMANDED

v.)

CENTOCOR ORTHO BIOTECH, INC. AND)
CENTOCOR BIOLOGICS, LLC,)

Defendant.)

**CENTOCOR'S REBUTTAL TO ABBOTT'S OPPOSITION TO
CENTOCOR'S MOTION TO AMEND ITS CLAIM CONSTRUCTION PLEADING**

Centocor is seeking leave to file this short rebuttal to Abbott's Opposition to Centocor's Motion to Amend Its Claim Construction Pleading. Although Centocor does not agree with Abbott's substantive position on claim construction, the Court has not invited a formal reply on that. Centocor nonetheless considers this short rebuttal to be necessary to address certain misleading or erroneous factual assertions made by Abbott in its Opposition (D.I. 132) concerning the issue of alleged prejudice.

I. Abbott Has *Not* Been Denied Fact Discovery Concerning Centocor's Germline Analysis

In its brief, Abbott argues that it has been prejudiced because, if it had known about the human antibody/germline issue earlier, it would have taken discovery about the document attached as Exhibit 10 to the Gunther declaration (Abbott Br. at 6). But Abbott *did* take discovery about this document. In fact, Abbott took a deposition of the author of this document *after* Centocor raised the issue about needing the Court to construe the term "human antibody" with reference to a germline sequence. Specifically:

1. On January 31, 2011, Centocor sent a letter alerting Abbott of the need to define the term "human antibody" with reference to a germline sequence (Pearson¹ Decl. Ex. 9)
2. On February 11, 2011 Abbott took the deposition of the author of Gunther Ex. 10, Tom Nesspor, a Centocor Scientist. Abbott specifically asked Mr. Nesspor about the comparison between the Centocor 12B75 antibody² and a germline sequence through several series of questions, excerpted below:

Q: So just reading the figure legend for Figure 2, the first sentence, does it state, the top portion shows a comparison of the 12B75 heavy chain variable region sequence to the DP-73 germline variable region sequence?

A: Yes, that's what's stated.

¹ The "Pearson Decl." and exhibits thereto were submitted with Centocor's Motion to Amend Claim Construction Pleadings filed on February 23, 2011 (D.I. 120 and 121).

² 12B75 is another name for Centocor's Stelara antibody, which is the product accused of infringement.

Q: And this comparison of the 12B75 sequence to the DP-73 sequence, how was that comparison performed?

A: I believe it was performed using a computer program which aligns amino acid sequences based on their similarity.

(Ex. A, Nesspor Tr. at 106:3-14; objection omitted).

Q: So if we look at the 12B75 amino acid sequence shown here, can you explain to me what is represented by these various dots and letters?

A: Yes, I can. The germline sequence is given on the top next to where it says 12B75. Anywhere that the 12B75 amino acid matched the germline sequence in that position, a dot was shown signifying that it was the same amino acid. Anywhere that there was a difference between the germline sequence and the sequence of 12B75, the difference that – the amino acid that differed was shown.

(*Id.* at 107:14 – 108:2).

Q: Did you expect to see differences between the 12B75 sequence and the DP-73 germline sequence?

A: Yes, we expected to see differences.

Q: Why did you expect to see differences?

A: Antibodies which have gone through the process of affinity maturation to bind to a specific antigen, part of that affinity maturation involves the mutation of amino acids to be different than the germline sequence.

(*Id.* at 108:18 – 109:6; objections omitted).

Q: Do you know why you compared this 12B75 sequence to DP-73 in particular as opposed to any of the other germline variable sequences?

A: My recollection is that we compared the 12B75 heavy chain variable region sequence to all of the germline sequences that we were aware of in the GenPharm mice, and that the DP-73 germline sequence was, had the greatest homology to the 12B75 sequence.

(*Id.* at 111:10-17).

Q: So this figure [Figure 3] also demonstrates a comparison of the 12B75 sequence to a germline sequence; is that correct?

A: Yes.

Q: And how does this differ from what's shown in Figure 2?

A: This is the light chain amino acid sequence compared to a light chain germline sequence, and Figure 2 was a heavy chain amino acid sequence compared to a heavy chain germline sequence.

(*Id.* at 112:22 – 113:10; objection omitted).

It is misleading, at best, for Abbott to suggest that it is somehow prejudiced because it was denied the opportunity to take fact discovery concerning Centocor's own germline analysis.³

II. Abbott Refused To Provide Discovery On Germline Analyses By Characterizing It As Expert; Abbott Takes A Completely Contrary Position Now To Claim Prejudice

Abbott now says that it is prejudiced because it would have taken fact discovery on the germline issue if it had been raised earlier (Abbott Br. at 5-6). But, during fact discovery, Abbott refused to answer Centocor's requests seeking information about the germline issue because Abbott claimed that this should be the subject of expert – not fact – discovery.

Centocor interrogatories 18 and 19 (served on January 20, 2011) sought Abbott's comparison of the accused antibody's sequence to a human germline sequence. Abbott refused to provide any substantive response, instead objecting to the requests as "seek[ing] information that is not relevant to any claim or defense in this action"⁴ and "premature to the extent it calls for expert discovery or an expert opinion" (Ex. B, Abbott's Objections to Sixth Set of Interrogatories at 7-9). Now, in its opposition, Abbott takes the directly contrary position, arguing that it has been prejudiced for not taking fact discovery on this exact subject. This complete turnabout in position should not be credited. Abbott cannot have it both ways — it

³ If Abbott thought that the document attached as Gunther Ex. 11 was also relevant, it could have asked Mr. Nesspor about that, as well. But Abbott chose not to do so despite its clear awareness that Centocor was raising the "human antibody" issue with the Court.

⁴ As Centocor explained to Abbott during a meet and confer about Abbott's refusal to provide the requested discovery, regardless of the outcome of Centocor's present motion, the information is relevant to Centocor's written description defense.

cannot avoid fact discovery by saying it is an issue for expert analysis and then claim prejudice for not pursuing fact discovery on this subject.⁵

III. Abbott Has Not Been Denied the Opportunity to Take Discovery of Centocor's Witnesses as to What the Term "Human" Means

Abbott has not been denied the opportunity to take discovery about how Centocor's witnesses have used the term "human antibody." To the contrary, as Abbott admits in its brief, it did ask several Centocor witnesses what the term "human" means in relationship to the phrase "human antibody" (Abbott Br. at 17). Although Centocor disagrees that the way Centocor employees use the term should have any bearing on how that term is defined by and used in the patents-in-suit, Abbott has had ample opportunity to explore this issue throughout discovery. In addition to the examples of testimony acknowledged by Abbott in its brief, Abbott also elicited the following testimony from current and former Centocor employees whom Abbott deposed as fact witnesses:

1. From the deposition of John Ghrayeb:

Q. Do you recognize this as an e-mail from you to David Knight and others on January 2nd, 2003?

A. Yes, in response to, you know, other e-mails.

Q. Would you take a moment and just read through the two previous e-mails in the chain.

Q. If I understand the comment you make at the top of the e-mail chain, you note that in your experience, quote, if you own it, what you call it is what it is. Can you briefly explain that?

A. It's probably a very flippant remark based on my biases. But, you know, I've seen people call antibodies fully human, including companies we both know, that,

⁵ Given Abbott's position now that this is appropriate fact discovery, Centocor will need to file a motion to compel a response to its Interrogatories 18 and 19.

you know, stretches the definition of the purest -- you know, what is human? Human is something that comes from you and me. And I think that's kind of what my, my definition of human versus humanized.

(Ex. C, Ghrayeb Tr. at 137:2-7; 138:5-15).

2. From the deposition of Jill Giles-Komar:

Q. Do you distinguish humanized antibodies from fully human antibodies?

A. I do, yes.

Q. And what is the distinction in your mind between those two?

A. A fully human antibody is an antibody that's human of origin.

Q. It starts out from the get-go as a human antibody?

A. It comes from human DNA, human -- that's my understanding.

(Ex. D, Giles-Komar Tr. at 15:21-16:6)

3. From the deposition of David Knight:

Q. Going back to the first one you mentioned, CNTO 888, is that a human antibody?

A. I think I would need to ask you to define human.

Q. Okay. Well, let me ask you what your definition of human antibody is.

A. Well, I use as a working definition basically the similarity of amino acid sequence between the antibody in question and the human antibody database and whether the similarity to that database is in the same range as the similarity of authentic human antibodies that are not -- I mean, that are derived from human B cells.

(Ex. E, Knight Tr. at 36:15-37:5).

These are just a few excerpts of testimony demonstrating that Abbott did take discovery about how the term "human antibody" was used by various witnesses.

IV. Abbott's Characterization of the Kabat Reference Is Inaccurate

Abbott suggests that there would be delay in the case because the Centocor antibody amino acid sequence would need to be compared to over 2500 pages in the 1991 version of the Kabat book (Abbott Br. at 7). But only about 150 pages of the Kabat book are directed to human antibody amino acid sequences. Specifically, there are about 75 pages of human heavy and light chain variable region sequences and about 75 pages of human constant region sequences. Accordingly, the time to do this comparison should not cause any delay in these proceedings, particularly since Abbott obviously already has a copy of the relevant publication.

V. Abbott Appears to have Mischaracterized the Court's Decision in the *Bayer v. Abbott* case

Centocor was not present at the hearing where the Court considered Abbott's attempt to unilaterally amend its contentions in the *Bayer v. Abbott* case (Abbott Br. at 1-2). But the hearing transcript (provided to Centocor for the first time as Gunther Exhibit 1 to Abbott's opposition) shows that Abbott **had not asked** the Court for leave to amend its contentions, as Centocor has done in this case. As the Court stated in the transcript provided by Abbott:

...and it seems to me that the thing to do when my court order says "this is the deadline" is to either seek clarification if you want a window later on or seek leave to amend. There's a – certainly a strong likelihood that I would grant a request for leave to amend. It is my general view that cases ought to be decided on the merits and not according to strict adherence to deadlines if justice requires otherwise, but there is a quality here that Abbott more or less did it unilaterally and did so at a point where it put Bayer at something of a disadvantage.

(Gunther Ex. 1, Hearing Tr. at 5:11-21).

The situation here is, accordingly, not analogous to that in the *Bayer v. Abbott* case, as Abbott suggests. Instead, contrary to the unilateral actions of Abbott in the *Bayer* case, Centocor promptly put Abbott on notice of its position well within the fact discovery period and before the Court had even issued its claim construction order. Centocor also sought leave to amend its

claim construction pleadings to seek construction of one additional term. This sequence of events was apparently not followed by Abbott in the *Bayer* case and its suggestion that Centocor's actions are on par with what occurred there are unfounded. In the end, this case ought to be decided on the merits.

Respectfully submitted,

Date: March 10, 2011

By: 

Dianne B. Elderkin (*pro hac vice*)

delderkin@akingump.com

Barbara L. Mullin (*pro hac vice*)

bmullin@akingump.com

Steven D. Maslowski (*pro hac vice*)

smaslowski@akingump.com

Angela Verrecchio (*pro hac vice*)

averrecchio@akingump.com

Matthew A. Pearson (*pro hac vice*)

mpearson@akingump.com

AKIN GUMP STRAUSS HAUER & FELD LLP

Two Commerce Square

2001 Market Street, Suite 4100

Philadelphia, PA 19103-7013

215-965-1200

FAX: 215-965-1210

Heather P. Repicky (BBO # 663347)

NUTTER MCCLENNEN & FISH LLP

World Trade Center West

155 Seaport Boulevard

Boston, MA 02210

617-439-2000

FAX: 617-310-9000

Attorneys For Defendants

CENTOCOR ORTHO BIOTECH, INC. and

CENTOCOR BIOLOGICS, LLC

CERTIFICATE OF SERVICE

The undersigned hereby certifies that a true and correct copy of the foregoing Defendants' Rebuttal to Abbott's Opposition to Centocor's Motion to Amend Its Claim Construction Pleadings was electronically mailed to counsel of record on March 10, 2011 through the Court's ECF notification system.

A handwritten signature in black ink, appearing to read "Angela Verrecchio", is written above a horizontal line.

Angela Verrecchio